Converging Methodologies for Assessment of Cognitive Development in Children with HPE

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Holoprosencephaly (HPE) is a developmental neural tube disorder that results in mild to severe agenesis of the brain, due to incomplete cleavage of the embryonic forebrain into cerebral hemispheres during the second month of pregnancy [1]. Children with HPE have multiple medical issues and often present with severe motor impairment and little or no expressive language. The assessment of these children using standard cognitive assessments is often not possible and thus their cognitive capacities are still largely unexplored.

The feasibility of using a range of converging techniques, including habituation, operant conditioning, and EEG/ERP procedures, to assess individual childrenís performance with a wide range of stimuli is demonstrated [2,3,4] The resultant battery allows more comprehensive evaluation of a childís strengths and weaknesses across a number of areas. These include executive function, speed and efficiency of information processing, short- and long-term memory, receptive language, symbolic skills, contingency learning, and phonological discrimination. In addition, the measurement of brain responses to differing stimuli circumvents the need for a child to communicate and therefore has good potential for assessing cognitive skills. For example, event-related brain potentials (ERPs) can be used to identify which stimuli a childís brain can discriminate, and techniques can be developed to assess more sophisticated skills such as vocabulary [5]. Much basic research remains to be done to establish developmental norms and to allow interpretation of what different ERP profiles might reflect in terms of concurrent and future cognitive skills. Nevertheless, techniques that can be used to analyze individual performance are under development. Summary profiles of cognitive development in children with HPE using a variety of tasks will be presented and discussed.

We also use strategies to evaluate patterns of brain activation (e.g. mismatch negativity [MMN] to rapid auditory sequences, topographical localization of brain areas activated across time, and direction, time course, and amplitude of brain activation to varying stimuli) and examine their relations with behavioral performance in children with HPE as compared to controls [6]. Data from 6 children with Semi-Lobar HPE as compared with age-matched and performance-matched controls will be shown that suggests marked differences in brain activation to auditory discrimination of complex tone-pairs. ERPs were recorded to a 100-100 Hz standard and to a 100-300 Hz deviant stimuli (15%) in a MMN paradigm. Interstimulus intervals within a tone-pair were either 300 or 70 ms. ERP peak amplitude and latency measures were calculated from difference waves (deviant ñ standard). Analyses revealed that the ERP waveform for the standard stimuli was similar in amplitude, latency and topographical distribution to that of control children. However for the deviant stimuli, an MMN-like waveform was observed at prefrontal and frontal regions, but with longer latency, suggesting alterations in sensory memory. Moreover, directed coherence analyses suggested that signals propagated between left and right frontal areas use the same frequency band at a similar intensity in both HPE and control children, however, a laterality effect was only seen in control children. Thus the signal propagation process in the HPE children differed from normal controls. These findings will be discussed further, however, ERPs appear to provide a viable technique for assessing early cognitive and memory processes when use of behavioral measures may be limited.

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